

EXHIBIT 6

**Charles
Schwamlein/LAKE/PPRD/ABBOTT**

03/03/2004 10:40:14 PM GMT

To "Holmes, Lewis Ball,M.D." <LHOLMES@PARTNERS.ORG>
cc
bcc
Subject Re: Date of next meeting and new abstract

Lew,

Thanks for the communication. Yes, we have a comment and understand that a substitute abstract may be submitted in view of the fact that the situation did not allow you to give a months notice as previously planned.

My only comment concerns the last sentence. In considering the alternatives to valproate, there is little information since the registry has not yet found any drugs to be safe, as such. It's only that the data regarding phenobarbital and valproate have been analyzable because of numbers.

The finding of safe drugs versus drugs with associated teratogenicity is the objective of the registry. At this point the registry has found data regarding valproate, but it has not found that that the specific alternative treatments for epilepsy are safe.

We would propose that the sentence reads "When consulting women of childbearing age, risk of teratogenicity should be an important factor in selecting therapy."

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02/25/2004 11:37 AM

To: "Janet Cragan, M.D." <Jcragan@cdc.gov>, Margaret Jacobs <jacobsm@ninds.nih.gov>, "Mark Yerby, M.D." <yerby@mindspring.com>, "Robert Mittendorf, M.D., Dr.P.H." <rmitten@lumc.edu>, "W. Allen Hauser, M.D." <wahauser@optonline.net>, "Adrienne Rothstein, Pharm.D." <adrienne.rothstein@elan.com>, "Charles Schwamlein, MD, MPH" <charles.schwamlein@abbott.com>, "Javier Cid, M.D., M.P.H., Dr.Ph.H." <javier.cid@pharma.novartis.com>, "John G. Weil, M.D." <john.g.weil@gsk.com>, "Joseph Hulihan, M.D." <jhulihan@ompus.jnj.com>, "Leo J. Russo, Ph.D. (lrusso1@janus.jnj.com)" <lrusso1@janus.jnj.com>, "Louis Mini,

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cc: "Diego F. Wyszynski (dfw@bu.edu)"
<dfw@bu.edu>, "Nambisan, Maya"
<MNAMBISAN@PARTNERS.ORG>
Subject: Date of next meeting and new
abstract

To: Members of the Scientific Advisory and Steering Committees
From: Lewis Holmes
Cc: Diego Wyszynski, Maya Nambisan
Re: Date of next meeting and new abstract
Date: February 25, 2004

1. We had suggested Wednesday, June 9 - Thursday, June 10th as the next meeting. Mark Yerby has a conflict with June 9th, but could meet on Thursday, June 10th - Friday, June 11th.

No one else indicated any conflicts for June 9-10. So, let's meet on June 10-11, 2004 in Boston.

Conflicts? Please respond ASAP.

2. Abstract: Rachel Alsdorf is a student at Boston University, who has been working with Diego on the compilation of the findings in VPA-exposed pregnancies. We decided to submit the enclosed abstract to the annual meeting of the Teratology Society.

The abstract is essentially the abstract of the manuscript under revision by Diego. 12 of you have provided comments on the manuscript; these comments have been considered in writing the manuscript, including the abstract.

Normally we plan to circulate an abstract one month before it is to be submitted to a meeting. Due to the last minute nature of the decision, we did not do that. However, if there is a concern about any sentence that the group wants changed, we will submit a substitute abstract. However, we should do this quickly, so the revised abstract is submitted before they are sent to the publisher.

If you have serious concerns about any part of the abstract, please send them to me as soon as possible. I will circulate them so we can develop a group consensus.

Thank you for your help.

Lew

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Title:	Evidence of Increased Birth Defects in the Offspring of Women Exposed to Valproate during Pregnancy: Findings from the AED Pregnancy Registry
Authors & affiliations:	Rachel M. Alsdorf ¹ , Diego F. Wyszynski ¹ , Lewis B. Holmes ^{2,3} , Maya Nambisan ³ , for the Antiepileptic Drug (AED) Pregnancy Registry ³ ¹ Genetics Program, Department of Medicine, Boston University School of Medicine; ² Genetics and Teratology Unit, Pediatric Service, Massachusetts General Hospital; ³ Department of Pediatrics, Harvard Medical School, Boston, Massachusetts
Abstract: (Your abstract must use Normal style and must fit in this space)	<p>Introduction: Valproic acid is widely used as an effective anticonvulsant, anti-migraine agent, and in the management of bipolar disorders. All of these conditions occur frequently in women of childbearing age. Monotherapy valproic acid (VPA) use during the first trimester of gestation has been associated with an increased risk for spina bifida and other major congenital anomalies in the newborn. However, most studies have been hampered by a small number of exposed pregnancies and a retrospective design.</p> <p>Methods: Data were collected by the Antiepileptic Drug (AED) Pregnancy Registry from pregnant women throughout the U.S. and Canada who were taking an anticonvulsant drug. The prevalence of congenital malformations among offspring of monotherapy VPA exposed women was compared to that among infants of women exposed to all other AEDs ("internal comparison group"), and to that among newborns in the Active Malformations Surveillance Program at Brigham and Women's Hospital ("external comparison group").</p> <p>Results: Sixteen affected cases were identified among 149 VPA exposed women (proportion: 10.7%, 95% confidence interval [CI]: 6.3-16.9%). The prevalence in the internal comparison group was 2.9% (95% CI: 2.0-4.1%; odds ratio: 4.0, 95% CI: 2.1-7.4; $p < 0.001$). Assuming a 1.62% prevalence in the external comparison group, the relative risk to having an affected offspring for VPA-exposed women was 7.3 (95% CI: 4.4-12.2; $p < 0.001$).</p> <p>Discussion: Maternal exposure to VPA during the first trimester of pregnancy significantly increases teratogenicity in humans. When consulting women of childbearing age, alternate therapies should be considered.</p>

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